Off-pump bilateral internal thoracic artery grafting in patients with left main disease

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Objective: This study assessed the safety and efficacy of off-pump bilateral internal thoracic artery grafting in patients with left main disease.

Methods: We reviewed the records of 768 patients who underwent off-pump bilateral internal thoracic artery grafting between September 2004 and June 2009. Bilateral internal thoracic artery grafts were used for the left coronary system in all patients, of whom 268 had left main disease and 500 did not. We compared operative and postoperative variables and early and 1-year angiographic patency rates of the bilateral internal thoracic artery between the 2 groups.

Results: The perioperative mortality and incidence of postoperative complications were not significantly different between groups. In patients without left main disease, the left and right internal thoracic arteries were used for the left anterior descending artery in 87.4% and 12.2% of patients, respectively. In patients with left main disease, the left and right internal thoracic arteries were used for the left anterior descending artery in 70.5% and 29.1% of patients, respectively. In patients with left main disease, the patency rates for the left and right internal thoracic arteries at 1-year postoperative follow-up were 97.0% and 93.2%, respectively. In patients without left main disease, the patency rates for the left and right internal thoracic arteries at 1-year follow-up were 97.6% and 91.6%, respectively. The patency rates of the left and right internal thoracic arteries did not differ significantly in patients with or without left main disease ($P = .9803$ and $P = .7205$ in left and right internal thoracic arteries, respectively).

Conclusions: Off-pump bilateral internal thoracic artery grafting was safe and effective in patients with left main disease. The patency rates of both grafts were comparable to those of patients without left main disease. (J Thorac Cardiovasc Surg 2010;140:1040-5)

Coronary artery disease (CAD) with left main disease (LMD) has historically been considered to carry a higher operative risk in coronary artery bypass grafting (CABG) than CAD without LMD.^{1,2} Recent advancement in operative techniques and perioperative management has enabled surgeons to perform CABG safely in patients with LMD. Generally, off-pump CABG is not preferred in patients with LMD because the displacement of the heart could cause torsion of LMD and acute hemodynamic deterioration.³ Some investigators have reported the safety of off-pump CABG in patients with LMD in studies with a relatively small sample size.⁴⁻⁷

Bilateral internal thoracic artery (ITA) grafting for revascularization has better survival benefits than single ITA

grafting,⁸ and patency rates and survival benefits are satisfactory when bilateral ITA grafts are used for the left coronary system.⁹ The combination of off-pump CABG with bilateral ITA grafting also yields favorable outcomes.¹⁰ However, the rate of bilateral ITA use is still low.¹¹

The aims of the present study are to assess the safety and efficacy of off-pump bilateral ITA grafting in patients with LMD and to assess early and 1-year angiographic results of bilateral ITA grafts in these patients.

PATIENTS AND METHODS

Patient Population

Between September 2004 and June 2009, 930 patients underwent isolated CABG at Sakakibara Heart Institute. Of those, 884 patients (95.1% of all isolated CABG cases) underwent isolated off-pump CABG and 768 patients (86.9% of all isolated off-pump CABG cases) underwent off-pump bilateral ITA grafting (Table 1). Table 2 shows the preoperative characteristics of these 768 patients, of whom 268 had LMD (LMD group) and 500 did not have LMD (non-LMD group). LMD was defined as the presence of 50% or greater stenosis in any angiographic view according to the Society of Thoracic Surgeons database.

Operation

General anesthesia was induced with midazolam (0.2 mg/kg) and fentanyl (4 µg/kg). Neuromuscular block was achieved with vecuronium

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Abbreviations and Acronyms

CABG = coronary artery bypass grafting
 CAD = coronary artery disease
 ITA = internal thoracic artery
 LAD = left anterior descending
 LMD = left main disease

(0.1 mg/kg). After intubating the trachea, the lung was ventilated with 2% to 2.5% of sevoflurane with an air-oxygen mixture. Nicorandil and landiolol, a short-acting beta-one selective antagonist, were administered throughout the operation. Anticoagulation was achieved with heparin at 300 U/kg after all grafts were harvested for coronary revascularization. Phenylephrine was continuously administered during distal coronary anastomosis to maintain the mean blood pressure at more than 60 mm Hg without accelerating the heart rate. Beta-agonists were administered after the proximal anastomosis if necessary. There was no difference in anesthetic methods in patients with and without LMD.

Bilateral ITA grafts were routinely used in patients who required revascularization of both the left anterior descending (LAD) artery and left circumflex artery territories. Bilateral ITAs were used as in situ grafts in preference to free grafts. In general, the left ITA was used for revascularizing the LAD and the right ITA was used for revascularizing the circumflex artery territory or diagonal branch. However, in patients with unstable hemodynamics caused by critical LMD, the LAD was revascularized with the right ITA first and then the circumflex artery territory with the left ITA. When multiple grafting was necessary in the circumflex artery territory, multiple sequential grafting was applied with the free right ITA. The left ITA was used as an in situ graft in 760 patients (99.0%) and as a free graft in 8 patients (1.0%). The right ITA was used as an in situ graft in 582 patients (75.8%) and as a free graft in 186 patients (24.2%). When the free right ITA was anastomosed to the ascending aorta, an intraoperative epiaortic ultrasound was routinely used to detect a disease-free area of the aorta. When the free right ITA was anastomosed proximally to another graft (left ITA, radial artery, or saphenous vein graft), a Y-composite graft was created.

The operative technique of off-pump CABG has been described.¹² All arterial grafts were harvested in a skeletonized fashion using an ultrasonic scalpel (Harmonic Scalpel, Ethicon Endosurgery, Cincinnati, OH). We grafted all significantly diseased coronary vessels (at least a 50% diameter reduction) larger than 1 mm in diameter. Long segmental reconstruction was performed when the LAD was diffusely diseased or the septal and diagonal arteries were affected by severe atheromatous plaques. An arteriotomy was extended proximally and distally to the intact segment of the LAD. Endarterectomy was performed if the atheromatous plaque was circumferential or too hard to pass a needle through. The left ITA was anastomosed to the LAD with a long onlay patch technique using 7-0 and 8-0 polypropylene running sutures. The detailed technique and outcomes of long segmental reconstruction of the LAD have been described.¹³

Angiography

Early postoperative angiography was performed in 615 patients (80.1%) after obtaining written informed consents. The median time to an early postoperative angiography was 10 days after surgery (range 1–20 days). If patients became symptomatic during a follow-up period, a diagnostic angiography was performed at that time. Unless patients became symptomatic within 1 year after surgery, a follow-up angiography was performed at 1 year after surgery. Follow-up postoperative angiography was performed in 381 patients (49.6%), and the median time was 12.2 months after surgery (range 2–21 months). Of these patients, 352 (45.8%) underwent both early and 1-year angiographic studies.

TABLE 1. Distribution of patients undergoing isolated coronary artery bypass grafting

	Single ITA	Bilateral ITA	Total
On-pump CABG	22	24	46
Off-pump CABG	116	768	884
Total	138	792	930

CABG, Coronary artery bypass grafting; ITA, internal thoracic artery.

Preoperative, intraoperative, postoperative, and angiographic variables were compared in patients with LMD and without LMD. The institutional review board approved this retrospective study and waived the need for written consents.

Nonelective operations included both emergency and urgent cases according to the definition of the Society of Thoracic Surgeons database. Operative death was defined as death occurring within 30 days after surgery. Low-output syndrome was defined as the postoperative need for any dose of adrenaline or more than $5 \mu\text{g/kg}^{-1}/\text{min}^{-1}$ of dopamine or dobutamine. Perioperative myocardial infarction was defined as a positive result for new Q waves in an electrocardiogram or a peak creatine kinase MB level of greater than 10% of total creatine kinase. Respiratory failure was defined as requiring prolonged ventilation (>48 hours) or having pneumonia. A postoperative cerebrovascular accident was defined as having a new stroke or intracranial bleeding confirmed by computed tomography. In patients with preoperative stroke, postoperative stroke was defined as a worsening of the neurologic deficit with new radiologic findings.

Patent graft was defined as a graft without occlusion, significant stenosis (>90%), or string sign. String sign was defined as luminal narrowing throughout the entire conduit, including stenosis of 90% or greater.

Early and 1-year patency rates were calculated by dividing the number of patent grafts by the total number of grafts. If patients with early nonpatent grafts underwent a 1-year angiogram, those nonpatent grafts were also counted as 1-year nonpatent grafts.

Statistical Analysis

All statistical analyses were performed using StatView 5.0 software (SAS Institute Inc, Cary, NC). Continuous variables are reported as the mean $\pm$ standard deviation if they are normally distributed. Otherwise, they are reported as a median. Continuous variables were compared by the Student *t* test, and discrete variables were compared by the chi-square test or Fisher's exact test. Actuarial event-free survival curves were estimated by the Kaplan-Meier method. The log-rank test was used to assess whether there was a difference in survival between subject groups.

RESULTS

Clinical Outcomes

Preoperative characteristics of both groups are shown in Table 2. Patients with LMD were older than those without LMD ($P = .0226$). The rate of unstable angina ($P = .0010$) and the mean Canadian Cardiovascular Society class ($P = .0079$) were higher in patients with LMD than in those without LMD. The mean number of diseased vessels was larger in patients without LMD than in those with LMD ($P = .0117$). Preoperative ejection fraction ($P = .0492$) and creatinine levels ($P = .0318$) were significantly better in patients with LMD than in those without LMD. More patients without LMD had a history of congestive heart failure ($P = .0359$), prior myocardial infarction ($P = .0002$), previous stroke ($P = .0326$), and diabetes mellitus ($P = .0281$) than those with LMD. More patients with

TABLE 2. Preoperative variables

	All	LMD group	Non-LMD group	P value
No.	768	268	500	
Age, y	68.0 ± 9.5	69.1 ± 9.7	67.4 ± 9.3	.0226
Gender, female	141 (18.4%)	56 (20.9%)	85 (17.0%)	.2182
Body surface area (m ²)	1.7 ± 0.2	1.7 ± 0.2	1.7 ± 0.2	.6108
Unstable angina	239 (31.1%)	104 (38.8%)	135 (27.0%)	.0010
CCS	2.3 ± 0.9	2.4 ± 0.9	2.2 ± 0.9	.0079
Ejection fraction (%)	56.1 ± 11.8	57.3 ± 11.3	55.5 ± 12.0	.0492
Diseased vessels	2.8 ± 0.4	2.8 ± 0.4	2.8 ± 0.4	.0117
Previous PCI	222 (28.9%)	74 (27.6%)	148 (29.6%)	.6165
Congestive heart failure	103 (13.4%)	26 (9.7%)	77 (15.4%)	.0359
Prior myocardial infarction	363 (47.3%)	102 (38.1%)	261 (52.2%)	.0002
Hypertension	513 (66.8%)	174 (64.9%)	339 (67.8%)	.4679
Diabetes mellitus	361 (47.0%)	111 (41.4%)	250 (50.0%)	.0281
Insulin	79 (10.3%)	13 (4.9%)	66 (13.2%)	.0005
Hyperlipidemia	470 (61.2%)	172 (64.2%)	298 (59.6%)	.2446
Smoking	461 (60.0%)	156 (58.2%)	305 (61.0%)	.4995
Previous stroke	95 (12.4%)	24 (9.0%)	71 (14.2%)	.0326
Peripheral vascular disease	68 (8.9%)	21 (7.8%)	47 (9.4%)	.5525
Creatinine (mg/dL)	1.2 ± 1.3	1.0 ± 0.8	1.2 ± 1.6	.0318
COPD	31 (4.0%)	9 (3.4%)	22 (4.4%)	.6122
Nonelective	93 (12.1%)	54 (20.1%)	39 (7.8%)	<.0001
Preoperative IABP use	46 (6.0%)	29 (10.8%)	17 (3.4%)	<.0001
Redo	6 (0.8%)	2 (0.7%)	4 (0.8%)	>.9999

CCS, Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; IABP, intraaortic balloon pump; LMD, left main disease; PCI, percutaneous coronary intervention.

LMD had emergency or urgent operations ($P < .0001$) and preoperative use of intraaortic balloon pump ($P < .0001$) than those without LMD.

Target coronary artery vessels of left and right ITA grafts are shown in Table 3. In patients with LMD, the right ITA was used as an in situ graft in 207 patients (77.2%) and as a free graft in 61 patients (22.8%). In patients without LMD, the right ITA was used as an in situ graft in 375 patients (75.0%) and as a free graft in 125 patients (25.0%). There was no statistical difference between the 2 groups in the in situ rate of right ITA ($P = .5472$).

In patients with LMD, left and right ITA grafts were used for the LAD in 189 patients (70.5%) and 78 patients (29.1%), respectively. In patients without LMD, left and right ITAs were used for the LAD in 437 patients (87.4%) and 61 patients (12.2%), respectively. The right ITA was used for the LAD more frequently in patients with LMD than in those without LMD ($P < .0001$). This tendency was also found when the target of the right ITA was compared between patients with unstable angina and patients with stable angina. The right ITA was more frequently used for the LAD in patients with unstable angina than in patients with stable angina (36.5% vs 24.4%, $P = .046$).

Operative and postoperative variables are listed in Table 4. Patients without LMD had a higher mean number of distal anastomoses per patient than those with LMD ($P = .0012$). The rate of long segmental reconstruction of the

LAD was higher in patients without LMD than in those with LMD ($P < .0001$). Patients without LMD had significantly longer operation times than those with LMD ($P < .0001$). The transfusion rate was significantly higher in patients with LMD than in those without LMD ($P = .0393$). The operative mortality and incidence of postoperative complications were not significantly different between the 2 groups.

During the follow-up period, 1 patient died of heart failure, 2 patients had recurrent angina, 4 patients had congestive heart failure, and 1 patient had a stroke in the group with LMD. Freedom from death and other cardiac or cerebrovascular events was $96.5\% \pm 1.2\%$ at 3 years. One patient died of heart failure, 3 patients had recurrent angina, and 9 patients had congestive heart failure in the group without LMD. Freedom from death and other cardiac or cerebrovascular events was $96.3\% \pm 0.9\%$ at 3 years. There was no significant difference between the groups regarding event-free rate ($P = .8603$).

Angiographic Outcomes

Early and 1-year postoperative angiograms were performed in 615 patients (80.1%) and 381 patients (49.6%), respectively. Table 5 lists the patency rates of the left and right ITAs at both early and 1-year angiographic studies.

In patients with LMD, the patency rates of the ITA grafts were 98.6% (left ITA) and 98.6% (right ITA) at early

TABLE 3. Targets of left and right internal thoracic artery grafts

	Left internal thoracic artery	Right internal thoracic artery	No.
LMD group (n = 268)	LAD	Diagonal branch	89 (33.2%)
	LAD	Circumflex artery	95 (35.4%)
	LAD	Inflow of other graft	5 (1.9%)
	Diagonal branch	LAD	8 (3.0%)
	Diagonal branch	Circumflex artery	1 (0.3%)
	Circumflex artery	LAD	66 (24.6%)
	Inflow of other graft	LAD	4 (1.4%)
Non-LMD group (n = 500)	LAD	Diagonal branch	202 (40.4%)
	LAD	Circumflex artery	211 (42.2%)
	LAD	Inflow of other graft	24 (4.8%)
	Diagonal branch	LAD	5 (1%)
	Diagonal branch	Circumflex artery	1 (0.2%)
	Circumflex artery	LAD	49 (9.8%)
	Circumflex artery	Diagonal branch	1 (0.2%)
	Inflow of other graft	LAD	7 (1.4%)

LAD, Left anterior descending artery; LMD, left main disease.

angiography and 97.0% (left ITA) and 93.2% (right ITA) at 1-year angiography. There were no significant differences in early ($P > .9999$) and 1-year ($P = .2547$) patency rates between the left and the right ITAs.

In patients without LMD, the patency rates of the ITA grafts were 99.0% (left ITA) and 99.3% (right ITA) at early angiography and 97.6% (left ITA) and 91.6% (right ITA) at 1-year angiography. Although there was no significant difference in the early patency rate ($P > .9999$) between the left and the right ITAs, there was a significant difference in the 1-year patency rate ($P = .0056$).

When patency rates of the left ITA were compared in patients with and without LMD, there were no significant differences in early ($P = .6999$) or 1-year ($P = .9803$) patency rates between the 2 groups. When the patency rates of the right ITA were compared in patients with and without LMD, there

were no significant differences in early ($P = .4264$) or 1-year ($P = .7205$) patency rates between the 2 groups.

DISCUSSION

The present study demonstrates the safety and efficacy of off-pump bilateral ITA grafting in patients with LMD. Furthermore, this study showed good early and 1-year patency rates of bilateral ITA grafts in this patient group.

The current gold standard of care for LMD is CABG. The American College of Cardiology/American Heart Association guidelines recognize only CABG as having a class IA indication for treatment of LMD.^{14,15} The evolution of surgical techniques and perioperative management has improved surgical outcomes. Percutaneous coronary intervention procedures recently have been performed for LMD and reported to have comparable results with

TABLE 4. Operative and postoperative data

	All	LMD group	Non-LMD group	P value
Anastomoses/patient	4.2 ± 1.2	4.0 ± 1.2	4.3 ± 1.1	.0012
Long segment reconstruction of LAD	309 (40.2%)	77 (28.7%)	232 (46.4%)	<.0001
Operation time (min)	279.5 ± 56.9	268.2 ± 56.8	285.5 ± 56.1	<.0001
Transfusion	268 (34.9%)	107 (39.9%)	161 (32.2%)	.0393
Intubation (h)	9.6 ± 14.8	10.0 ± 10.2	9.5 ± 16.8	.6485
Intensive care unit stay (d)	1.9 ± 7.8	2.6 ± 13.0	1.5 ± 1.8	.0598
Operative death (within 30 d)	7 (0.9%)	2 (0.7%)	5 (1.0%)	>.9999
Reexploration because of bleeding	6 (0.8%)	1 (0.4%)	5 (1.0%)	.6706
Low output syndrome	10 (1.3%)	6 (2.2%)	4 (0.8%)	.1055
Perioperative myocardial infarction	11 (1.4%)	4 (1.5%)	7 (1.4%)	>.9999
Severe ventricular arrhythmia	6 (0.8%)	0	6 (1.2%)	.0969
Atrial fibrillation	191 (24.9%)	66 (24.6%)	125 (25.0%)	.9789
Required hemodialysis	13 (1.7%)	7 (2.6%)	6 (1.2%)	.2492
Stroke	10 (1.3%)	3 (1.1%)	7 (1.4%)	>.9999
Mediastinitis	10 (1.3%)	3 (1.1%)	7 (1.4%)	>.9999

ITA, Internal thoracic artery; LAD, left anterior descending artery; LMD, left main disease.

TABLE 5. Cumulative angiographic patency rates of left and right internal thoracic artery grafts

	Early (n = 615)	1 y (n = 381)
Total	98.9% (1217/1230)	94.8% (722/762)
LMD group	98.6% (424/430)	95.1% (251/264)
Left internal thoracic artery	98.6% (212/215)	97.0% (128/132)
Right internal thoracic artery	98.6% (212/215)	93.2% (123/132)
Non-LMD group	99.1% (793/800)	94.6% (471/498)
Left internal thoracic artery	99.0% (396/400)	97.6% (243/249)
Right internal thoracic artery	99.3% (397/400)	91.6% (228/249)

LMD, Left main disease.

CABG;¹⁶ however, long-term results have not been reported. A meta-analysis of LMD also supports the superiority of CABG over percutaneous coronary intervention in revascularization of LMD; the study showed that repeated revascularization was less frequent after CABG than after percutaneous coronary intervention.¹⁷ Generally, off-pump CABG is not preferred in patients with LMD because displacement of the heart could induce hemodynamic deterioration.³ On the other hand, several studies have shown the safety and feasibility of off-pump CABG in patients with LMD.^{4,7} Dewey and colleagues⁶ reported that the use of cardiopulmonary bypass is an independent risk factor for death in patients with LMD, with an odds ratio of 7.3 (95% confidence interval, 1.3–138.4). Thomas and colleagues⁷ reported that off-pump CABG was safely performed in patients with and without LMD. They speculated that the favorable outcomes after off-pump CABG were achieved because of the improved myocardial preservation, reduced reperfusion injury, and absence of the hypothermic insult. Even in those series, bilateral ITA grafting was infrequently performed.

Several institutions have reported that bilateral ITA grafting results in better survival and greater freedom from reintervention than single ITA grafting.^{18,19} However, the American College of Cardiology/American Heart Association guidelines still do not recommend the use of bilateral ITA grafting because there are insufficient data for detailed analysis.¹⁴ Bilateral ITA grafting has not become a routine strategy, even in elective patients, for multiple reasons, including increased operative difficulty, increased operating times, and risk of wound complications.¹⁴ There are only a few reports regarding myocardial revascularization with bilateral ITA grafting in patients with LMD.²⁰ We have routinely used bilateral ITA grafts for CABG when feasible even in high-risk patients with LMD. There are various grafting strategies with bilateral ITA grafts. Although our first choice is the left ITA for the LAD, we use the right ITA for the LAD more frequently in those with LMD than in those without LMD. Patients with unstable hemodynamics cannot tolerate torsion of the left main trunk because of the circumflex position without LAD grafting. In those patients, we graft the LAD with the right ITA and then graft the circumflex territory with the left ITA. The left ITA to

the LAD would suffer from increased physical tension when the heart is pulled toward the right during the anastomosis of the circumflex territory. However, in patients with stable hemodynamics, revascularization of the LAD was performed with the left ITA as usual.

The present study used intraaortic balloon counterpulsation in a higher proportion of patients with LMD than in patients without LMD. Suzuki and colleagues²¹ demonstrated that using an intraaortic balloon pump during off-pump CABG was effective in high-risk patients. They comment that the effects of intraaortic balloon pump support, such as the reduction of ventricular afterload, improvement of diastolic coronary perfusion, and enhancement of subendocardial perfusion, are beneficial to the displaced heart in maintaining hemodynamic stability during off-pump CABG. These benefits may have influenced the favorable results after off-pump CABG in our study. In the present study, all intraaortic balloon pumps were placed preoperatively. We believe that insertion of an intraaortic balloon pump should not be delayed in hemodynamically unstable patients with LMD.

We have demonstrated that clinical and angiographic outcomes are not significantly different in patients with and without LMD at early and 1-year follow-ups. The 1-year patency rate of the right ITA graft was relatively low in patients without LMD. However, there was no significant difference in the patency rates of the right ITA grafts in patients with or without LMD.

We used the ITA as a skeletonized graft. A skeletonized ITA provides a longer length and better flexibility than a pedicled ITA. Skeletonization ensures that the right ITA reaches the posterolateral vessels through the transverse sinus as an in situ graft. Furthermore, multiple sequential grafting can be performed easily with a skeletonized free right ITA. With the skeletonization technique, using bilateral ITAs may no longer be a risk factor for mediastinitis because the collateral blood supply to the sternum is preserved.²² In the present study, the overall mediastinitis rate of 1.3% is not particularly high; however, the best practice in the literature is approximately 0.3%.²³ At Sakakibara Heart Institute, the mediastinitis rate in patients undergoing non-bilateral ITA grafting was 0% (0/116). However, there was no difference regarding the mediastinitis rate between patients with bilateral ITA and patients with non-bilateral ITA ($P = .3756$).

Study Limitations

Our study has the following limitations. It is a retrospective observational study, not a randomized controlled trial. We did not compare off-pump CABG with bilateral ITAs with other types of CABG (single ITA grafting or conventional on-pump CABG) in patients with LMD; however, at least we showed that our routine off-pump CABG with bilateral ITAs is safe and effective in patients with LMD. In addition, we did not follow up all patients with bilateral ITA

grafts. Our findings may not be applicable to patient groups who did not have a follow-up angiogram, namely, the elderly and patients with renal insufficiency.

CONCLUSIONS

Off-pump bilateral ITA grafting in patients with LMD can be performed safely with acceptable early and 1-year patency rates.

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